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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,353	04/27/2001	Gary Ruvkun	00786/351005	3561

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 05/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/844,353	RUVKUN ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *02 March 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☒ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See Continuation Sheet*.

3.☒ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1,2,4 and 12-15*.

Claim(s) withdrawn from consideration: *5-11*.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☒ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). *1,5,8*.

10.☐ Other: _____

JEFFREY FREDMAN
PRIMARY EXAMINER

Continuation of 2.
NOTE: Newly proposed claimed amendment "a gene that hybridizes under stringent conditions to SEQ ID NO:54 and that functions in insulin signaling" in claim 17 and its dependent claims 18-20 would require additional search and/or further consideration under 35 USC112(1) regarding Written description and Enablement issues.

Continuation of 5. does NOT place the application in condition for allowance because:
Claims 1, 2, 4 and 12-15 stand rejected under 35 USC 112(1) regarding written description and enablement issues for the same reasons of record as set forth in the office action mailed on 11/18/03.

Regarding written description issues, the applicant argues that after the recent amendment that limits invention to a method that requires a gene that encodes a polypeptide having 85% or 95% sequence similarity to the amino acid sequences of SEQ ID NO: 54. The amended claims now recite characteristic functional and structural features of DAF-16-related polypeptides, which clearly satisfy the written description requirement. The applicant argues that the applicants have demonstrated that the structural similarities between the members of the daf-16 family are echoed in functional relatedness. The applicant argues that although C. elegans and humans are evolutionarily distant organisms, C. elegans daf-16 and human proteins FKHR and AFX are highly related. The applicant argues that Dr. Ruvkun and his colleagues have shown that FKHR and DAF-16 are so closely related that the human protein is able to functionally substitute for C. elegans DAF-16 in vivo.

However, applicant's argument are found NOT persuasive because the scope of invention as claimed encompasses variants of SEQ ID NO:54 wherein in 10-15% of amino acid sequences are added, substituted or deleted over the entire length of the amino acid sequences of SEQ ID NO:54. Applicants were referred to the guidelines for *Written Description Requirement* published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110. Under the law the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case daf-16 gene (as claimed) has been defined only by a statement of a function that broadly encompasses activation of insulin growth factor binding protein response element, which conveyed no distinguishing information about the identity of the claimed genetic sequence, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Regarding enablement issues the applicant argues that the amended claims are limited to screening methods that requires having at least 85% amino acid identity to SEQ ID NO:54 and that functions in insulin signaling. The applicant argues that the proper test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with the information known in the art without undue experimentation. The applicant argues that at pages 76 and 77 of the specification, applicants disclose five amino acid sequences that may be used to identify a daf-16 family member present in a sequence database or that may be used to design degenerate probes to identify such a gene present in a

genomic or cDNA library. The applicant further argues that Dr. Ruvkun and his colleagues discloses that adaf-16 human homolog expressed under the control of daf-16b promoter in worms having mutation in daf-16 and daf-2 was able to functionally replace the worm protein. The applicant concluded that in view of above evidence that other variants of daf-16 family can be identified and tested for the daf-16 related function.

However, this is found NOT persuasive because the scope of invention as claimed is not limited to daf-16 gene. The scope of invention as claimed encompasses any natural and/or non-natural variant and/or homolog of daf-16 gene obtained form any organism that could be used to screen candidate compounds for ameliorating or delaying an impaired glucose tolerance condition, atherosclerosis or obesity. Even though making a transgenic *C. elegans* is routine in the art making a transgenic *C. elegans* with any variant or homolog of daf-16, wherein the structure and function of the transgene has not been define is not considered routine in the art, which requires undue amount of experimentation. Under the law, the disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the wands factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). In instant case screening of any and all natural and non-natural variants of daf-16, wherein at least 10-15% amino acids are added substituted and/or deleted in the disclosed SEQ ID NO:54 is not considered routine in the art, since making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein at least 10-15% amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the functional requirements for the claimed daf-16 activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.